

WHAT IS CLAIMED IS:

1. A composition comprising at least one covalent product of a target enzyme of a complex protein composition and at least one activity based probe member of a combinatorial chemical library comprising a plurality of members of the formula

R (F - L) -X

wherein:

X is a ligand, said ligand having the same chemical structure for each of said members of said library;

L is a bond or linking group, which is the same in each of the members of said library, and said linking group is of from 1 to 20 carbon atoms;

F is a sulphonyl group reactive at an active site of a target enzyme; and

R is an organic group of less than 1kDal, that is different in each of the members of the library and is bonded to F; and

wherein members of the library have different on rates with said target enzyme.

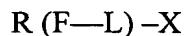
2. A composition according to Claim 1, wherein R is selected from the group consisting of alkyl, cycloalkyl, heterocycle and aryl and substituted members thereof.

3. A composition according to Claim 1, wherein said target enzyme is an aldehyde dehydrogenase.

4. A composition according to Claim 1, wherein said linking group is an aliphatic chain.

5. A composition according to Claim 1, wherein said linking group is an alkyleneoxy chain of from one to 6 alkyleneoxy groups, wherein said alkyleneoxy is of from 2 to 3 carbon atoms.

6. A compound of the formula:



wherein:

X is biotin;

L is alkylene or an alkyleneoxy chain of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms;

F is a sulphonyl group;

R is heteroaryl or aryl.

7. A compound according to Claim 6, wherein R is pyridyl.

8. A compound according to Claim 6, wherein R is thiophenyl.

9. A combinatorial chemical library comprising a plurality of members of the formula



wherein:

X is a ligand for binding to a reciprocal receptor;

L is alkylene or an alkyleneoxy chain of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms;

F is a sulphonyl group reactive at an active site of a target enzyme; and

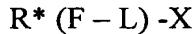
R is an organic group of less than 1kDal, that is different in each of the members of the library and is bonded to R; and

wherein members of the library have different on rates with said target enzyme.

10. A combinatorial library according to Claim 9, wherein R in one member of said library is pyridyl or thiophenyl.

11. A combinatorial library according to Claim 9, wherein said ligand is biotin.

12. A method for screening for molecules having an affinity for an active protein in a complex mixture of proteins from a biological source, employing a combinatorial chemical library comprising a plurality of members of the formula



wherein:

X is a ligand having the same chemical structure for each of said members of said library;
L is a bond or alkylene or an alkyleneoxy chain linking group of from 1 to 6 alkyleneoxy groups, wherein said alkyleneoxy groups are of from 2 to 3 carbon atoms, which is the same in each of the members of said library;

F is a sulfonyl functional group reactive at an active site of a protein member, which functional group comprises the same reactive functionality in each of the members of said library; and

R is a group of less than 1kDal, that is different in each of the members of the library;
the * intends that R is a part of F or L; and

wherein members of said library have different on rates with said protein member;
said method comprising:

(1) combining with said complex mixture, in an active form and an inactivated form, said combinatorial chemical library under conditions for reaction of said functional group with active proteins to form a conjugate;

(2) isolating conjugates from said active and inactivated complex mixture; and

(3) comparing conjugates formed with said active and inactivated complex mixtures;

whereby conjugates in said active complex mixture absent in said inactivated complex mixture are comprised only of active proteins reactive with members of said combinatorial library.

13. A method according to Claim 12, wherein each of said members of said combinatorial library is isotopically individually labeled, said method including the additional steps of:

isolating conjugates from said active complex mixtures; and

analyzing said conjugates for the composition of said probe by means of said isotopic individual label and for the composition of said protein by at least partial sequencing.